BMJ Open

Knowledge, attitude and practice towards chemotherapy-related neutropenia and febrile neutropenia among breast cancer patients

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To cite: Chen Y, Zhou H, Jiang J. Knowledge, attitude and practice towards chemotherapy-related neutropenia and febrile neutropenia among breast cancer patients. *BMJ Open* 2024;**14**:e089738. doi:10.1136/bmjopen-2024-089738

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2024-089738).

Received 07 June 2024
Accepted 04 October 2024

Check for updates

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ABSTRACT

Objectives This study aimed to investigate the knowledge, attitude and practice (KAP) towards chemotherapy-related neutropenia and febrile neutropenia (FN) among breast cancer patients. The major hypothesis was that demographic characteristics influence patients' KAP regarding chemotherapy-related neutropenia and FN.

Design A multi-centre cross-sectional study.

Setting Conducted in four secondary care hospitals between April and June 2023.

Participants The study enrolled 246 breast cancer patients undergoing chemotherapy. Participants were aged 18 years or older, currently on chemotherapy and willing to complete the questionnaire. Exclusion criteria included significant cognitive impairments.

Primary and secondary outcome measures Primary outcome measures were KAP scores regarding chemotherapy-related neutropenia and FN. Secondary outcomes included factors associated with adequate knowledge and positive attitudes.

Results A total of 246 patients completed the questionnaire. The mean knowledge score was 12.46±6.21 (range: 0–26), and the mean attitude score was 30.00±2.58 (range: 7–35). Less than half of the patients (45.95%) knew whether their chemotherapy protocol was high risk for FN, while 79.67% were aware of the need for prophylactic administration of leukocyte-raising agents. Multivariate logistic regression analysis revealed that having a junior college education or higher was significantly associated with knowledge scores (OR=4.69, 95% CI 2.23 to 9.89, p<0.001). Living in urban areas was associated with attitude scores (OR=0.58, 95% CI 0.34 to 0.97, p=0.037). Structural equation modelling analysis indicated that experience with chemotherapy-related neutropenia or FN influenced knowledge to some degree (β=1.77, p=0.029).

Conclusions The study found inadequate knowledge, a positive attitude and suboptimal practice towards chemotherapy-related neutropenia and FN among breast cancer patients undergoing chemotherapy. Tailored education programmes are needed to improve KAP in this patient population. Further research should explore additional demographic and psychosocial factors influencing KAP to develop comprehensive educational interventions.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The study's multi-centre approach enhances the generalisability of the findings across different hospital settings.
⇒ The use of a self-administered questionnaire to assess knowledge, attitude and practice provides a holistic understanding of patients' perspectives.
⇒ The application of structural equation modelling allows for a detailed analysis of the interactions between knowledge, attitude and demographic characteristics.

INTRODUCTION

Breast cancer remains a significant global health concern, affecting a large number of individuals worldwide.[1 2] With advancements in medical research and technology, chemotherapy has become a critical component of breast cancer treatment, leading to improved outcomes and increased survival rates for patients.[3 4] However, chemotherapy is not without its challenges, one of which is the risk of chemotherapy-related neutropenia and subsequent development of febrile neutropenia (FN).[5]

Neutropenia is characterised by a reduction in the number of neutrophils and crucial white blood cells that play a pivotal role in fighting infections. It can be a severe complication of chemotherapy.[6] When neutropenia is accompanied by fever, it leads to FN, a potentially life-threatening condition that requires immediate medical attention and intervention. The incidence of chemotherapy-induced neutropenia and FN among breast cancer patients is up to 31.9% and 5.3%, respectively,[6 7] and they are associated with a risk of life-threatening infections.[8] These complications often lead to treatment delays and dose reductions, negatively impacting treatment efficacy and compromising patient morbidity and survival.[7] To prevent chemotherapy-induced

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neutropenia/FN, primary prophylaxis with granulocyte colony-stimulating factor and prophylactic antibiotics are recommended in high-risk patients.[8 9]

Understanding the knowledge, attitude and practice (KAP) of breast cancer chemotherapy patients towards chemotherapy-related neutropenia and FN is crucial for improving patient care and safety during the course of treatment. Patients need adequate knowledge about the risks and potential complications associated with chemotherapy to make informed decisions and actively participate in their treatment plans. A positive attitude towards preventive measures and symptom recognition can help patients take appropriate actions and seek timely medical attention if complications arise. However, there is a lack of studies investigating the KAP in this population. Only one relevant study was identified, which surveyed Japanese malignant lymphoma patients receiving chemotherapy and found an inadequate level of awareness and poor practice towards FN.[10] While some research has been conducted on KAP related to chemotherapy-related complications,[11–13] there is a scarcity of data specifically focusing on breast cancer patients. Therefore, a study on KAP of neutropenia/FN among breast cancer chemotherapy patients is needed to address this research gap.

Therefore, this study aimed to assess the KAP towards chemotherapy-related neutropenia and FN among breast cancer patients.

MATERIALS AND METHODS

Study design and patients

This cross-sectional survey was conducted at West China Hospital of Sichuan University, Chengdu Shangjin Nanfu Hospital, the First Affiliated Hospital of Wenzhou Medical University and Quzhou People's Hospital between April 2023 and June 2023, and breast cancer patients who underwent chemotherapy were recruited. Inclusion criteria are as follows: (1) patients with a confirmed breast cancer diagnosis; (2) age 18 years or above; (3) have been treated with intravenous chemotherapy within the last 5 years and (4) voluntary participation in the study. Exclusion criteria is as follows: (1) suffering from psychiatric disorders or unable to answer the questionnaire. This study has been approved by the Medical Ethics Committee of Quzhou People's Hospital (No. 2023–024), and written informed consent was obtained from each patients.

Patient and public involvement

Patients were not involved in the planning of the study and designing the questionnaire, but before the study starts, they were invited to reliability and internal consistency test and encouraged to voice their opinions about the questionnaire. Participants also received special education regarding chemotherapy before the treatment start and were encouraged to share the contents of the study with their families and community. Participants who expressed the desire to learn more about the study were given a more detailed explanation and will be informed of the results after the study is published.

Questionnaire

The questionnaire was designed with reference to the Chinese Society of Clinical Oncology Guidelines on the Standardized Management of Radiotherapy and Chemoradiotherapy-related Neutropenia (2021) and previous literature.[14–16] The questionnaire design underwent two rounds of expert review. Three experts (two oncologists and one epidemiologist) were selected for the first round; a description of neutrophilic granulocyte (NE) and NF were added based on expert comments. Two new experts (one oncologist and one epidemiologist) were selected for the second round; knowledge items on the definition of NE and NF were removed, and items with ambiguities were clarified. A random sample of 32 individuals was selected for the reliability test, and the Cronbach's α coefficient was 0.8714, suggesting good internal consistency.

The final questionnaire (online supplemental materials) contained four dimensions: demographic information (eg, age, education, smoking history, alcohol consumption, breast cancer treatment status and incidence of chemotherapy-related neutropenia or FN), knowledge dimension, attitude dimension and practice dimension. The knowledge dimension consisted of 13 items, scoring 2 points, 1 point and 0 point for 'well known', 'partially known' and 'unknown', ranging from 0 to 26 points. The attitude dimension consisted of 7 items using a 5-point Likert scale ranging from strongly agree (5 points) to strongly disagree (1 point) with negative attitude items scored in reverse, ranging from 7 to 35 points. The practice dimension consisted of four items regarding whether the patient was informed about FN: (1) whether the chemotherapy protocol administered was a high-risk protocol for FN, (2) whether the high-risk protocol required prophylactic administration of leukocyte-raising agents, (3) whether subsequent chemotherapy required prophylactic administration of leucocyte-raising agents if FN has previously occurred and (4) whether the risk of FN should be assessed at each chemotherapy cycle. A descriptive analysis was performed for the practice dimension.

Adequate knowledge and positive attitudes are defined by having a score greater than 70% of the total score for each dimension.[17]

To distribute the questionnaire, it was uploaded to the Sojump website (https://www.wjx.cn/) to create a QR code for the electronic questionnaires. The research team contacted the department heads in hospitals and informed them of the study's purpose. With their cooperation, the electronic questionnaire was distributed to patients through WeChat. To prevent duplicate responses, internet protocol (IP) restriction was applied, allowing each survey to be completed only once from a single IP address. Study participants were randomly selected among breast cancer patients who were registered in the study hospitals and met the inclusion criteria, using

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random number table. Invitations to answer the questionnaire were sent using Wechat messenger or telephone. All data were anonymous. After collection, the questionnaires were reviewed for quality by six members of the research team. Questionnaires with obvious logical errors or a pattern of selecting the same options for all items were considered invalid and excluded from the analysis.

Statistical analysis

Stata 17.0 (Stata Corporation, College Station, TX, USA) was used for the statistical analysis. The sample size was calculated based on item-respondent theory, in which a ratio of 1:5 up to 1:20 is considered suitable.[18] Thus, a ratio of 1:10 was selected, and with 24 KAP items of the questionnaire (excluding demographics), the required sample size was 240. Taking potential refusals to participate into account, 270 patients were initially invited. Continuous variables were expressed as mean±SD, and comparisons between groups were performed by t-test or analysis of variance. Categorical variables were expressed as n (%). Variables with p<0.05 in the univariate analysis were included in the multivariate analysis, and demographic factors associated with knowledge and attitude were explored by using multivariate logistic regression analysis. The structural equation model (SEM) was constructed with the hypotheses that (1) knowledge would influence attitude towards chemotherapy-related neutropenia and FN and (2) menopause and the experience of chemotherapy-related neutropenia or FN would influence both knowledge and attitude. Two-sided p<0.05 was considered to be statistically significant.

RESULTS

A total of 3375 registered breast cancer patients across the three hospitals met the inclusion criteria, and 270 were selected using a random number table. Of the 270 patients contacted, 24 refused to participate, while 246 completed the questionnaire and were included in the analysis. Over half of the patients aged 50 years or above (56.50%), lived in rural areas (55.28%) and had a middle school level of education or below (57.72%). Most patients were non-smokers (98.78%) and non-drinkers (88.62%). Around half had already reached menopause (52.85%), and most of them had been diagnosed with breast cancer for less than 3 years (84.15%). More than one-third of the patients had suffered from chemotherapy-related neutropenia or FN (37.40%); among them, 8.7% had their chemotherapy drug adjusted, and 52.17% had their chemotherapy delayed (online supplemental table 1).

The mean knowledge score was 12.46±6.21 (possible range: 0–26), and the mean attitudes score was 30.00±2.58 (possible range: 7–35) (table 2). Significant differences in knowledge scores were observed based on age (p=0.004), residence (p=0.008), education (p<0.001) and those who suffered from chemotherapy-related neutropenia or FN (p<0.001). Significant differences in attitude scores were observed based on age (p=0.020), residence (p=0.021) and education (p=0.024).

The overall correct rate of the knowledge dimension was low, reflecting the inadequate knowledge regarding chemotherapy-related neutropenia or FN among breast cancer chemotherapy patients. The following three knowledge items had the highest correct rates: 'Do you know that neutropenia can be detected by routine blood tests?' (66.26%), 'Do you know that NE is a type of white blood cell?' (49.59%) and 'Do you know that your temperature needs to be measured routinely for 7–14 days after chemotherapy?' (49.19%). The following three knowledge items had the lowest correct rates: 'Do you know about the primary prevention measures for FN?' (10.16%), 'Do you know that advanced age and underlying diseases (eg, hypertension, coronary heart disease) increase the risk of neutropenia?' (13.82%) and 'Do you know that high chemotherapy doses and the combination of different chemotherapy drugs can cause neutropenia?' (17.89%) (online supplemental table 2).

The majority of the patients had a positive attitude. Nonetheless, 71.54% strongly agreed or agreed that 'I would be very anxious if neutropenia was screened', and 59.35% strongly agreed or agreed that 'I think that the high cost of treatment and prevention of neutropenia places a financial burden on me' (online supplemental table 2). Less than half of the patients knew whether their chemotherapy protocol was a high-risk protocol for FN (45.95%). However, the majority of patients were aware of the need for the prophylactic administration of leucocyte-raising agents (79.67%). And 79.27% patients reported being informed about the need for prophylactic administration of leucocyte-raising agents for subsequent chemotherapy if they had experienced FN in the past, but only 36.59% patients were informed that the risk of FN should be assessed at each chemotherapy cycle (online supplemental table 4).

Multivariate logistic regression analysis showed that junior college and above education (OR=4.69, 95% CI 2.23 to 9.89, p<0.001) were associated with knowledge scores (table 1). Living in urban areas (OR=0.58, 95% CI 0.34 to 0.97, p=0.037) was associated with attitude scores (table 2).

The SEM results showed that there was no direct effect of knowledge on attitudes (β= −0.05, 95% CI −0.10 to 0.002, p=0.058); menopause status had no direct effect on knowledge (β= −0.32, 95% CI −1.86 to 1.22, p=0.683); experience with chemotherapy-related neutropenia or FN had a direct effect on knowledge (β=1.77, 95% CI 0.18 to 3.36, p=0.029); menopause status and experience with chemotherapy-related neutropenia or FN had no direct effect on attitudes (β=0.16, 95% CI −0.48 to 0.80, p=0.618; β=0.55, 95% CI −0.11 to 1.22, p=0.103, respectively) (figure 1, table 3). The fitting indexes of the SEM, including root mean square error of approximation, comparative fixation index, Tucker–Lewis index and standardised root mean square residual, suggested a good model fit.

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Table 1 Multivariate analysis of factors associated with knowledge scores

Variables	Univariate		Multivariate	
	OR (95% CI)	P	OR (95% CI)	P
Age				
<50 years	Ref.			
≥50 years	0.63 (0.38, 1.05)	0.075		
Residence				
Rural	Ref.			
Urban	2.14 (1.28, 3.58)	0.004	1.25 (0.63, 2.47)	0.525
Education				
Middle school and below	Ref.			
High school/technical secondary school	0.78 (0.41, 1.49)	0.456	0.57 (0.27, 1.19)	0.137
Junior college and above	4.69 (2.23, 9.89)	<0.001	3.36 (1.34, 8.43)	0.010
Marital status				
Married	0.52 (0.24, 1.10)	0.087		
Unmarried/divorced/widowed	Ref.			
Childbirth				
Yes	1.43 (0.61, 3.35)	0.415		
No	Ref.			
Menopause				
Yes	1.26 (0.76, 2.08)	0.368		
No	Ref.			
Duration of breast cancer				
<3 years	Ref.			
≥3 years	0.75 (0.38, 1.50)	0.415		
Duration of chemotherapy for breast cancer				
<6 months	Ref.			
≥6 months	0.85 (0.47, 1.54)	0.590		
Chemotherapy-related neutropenia or febrile neutropenia				
Yes	1.49 (0.84, 2.66)	0.173	1.43 (0.78, 2.62)	0.247
No	Ref.			
Unclear	0.38 (0.19, 0.77)	0.008	0.39 (0.19, 0.83)	0.014

DISCUSSION

The present study demonstrated inadequate knowledge, positive attitude and suboptimal practice among breast cancer patients towards chemotherapy-related neutropenia and FN. Inadequate knowledge was significantly associated with a lower level of education and negative attitude was significantly associated with living in urban areas. Structural equation modelling found the experience with chemotherapy-related neutropenia or FN had a direct effect on knowledge. The findings can help clinicians and researchers to develop appropriate interventions to enhance the KAP of chemotherapy-related neutropenia and FN in this patient population.

The knowledge score revealed a low overall correct rate, indicating that breast cancer chemotherapy patients possess inadequate knowledge regarding chemotherapy-related neutropenia and FN. This finding aligns with several previous studies conducted in different cancer populations that have also reported suboptimal levels of knowledge regarding chemotherapy-related complications.[10 11 13] Arunachalam *et al* reported that 42% of chemotherapy patients had above-average level knowledge on chemotherapy side effects.[11] Similarly, Pathirana *et al* found that most chemotherapy patients at a teaching hospital had a very poor overall knowledge level regarding chemotherapy and its side effects.[13] Takamatsu *et al* demonstrated that 58.1% of lymphoma chemotherapy patients understood FN very well or almost well.[10] This outcome highlights the need to improve patient education related to chemotherapy-related complications, including neutropenia and FN.

The low correct rates for items related to primary prevention measures for FN and risk factors for neutropenia observed in our study are consistent with findings from other research studies. Haghpanah *et al* reported that 47% of breast cancer patients receiving chemotherapy

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Table 2 Multivariate analysis of factors associated with attitude scores

Variables	Univariate		Multivariate	
	OR (95% CI)	P	OR (95% CI)	P
Age				
<50 years	Ref.			
≥50 years	1.35 (0.81, 2.23)	0.252		
Residence				
Rural	Ref.			
Urban	0.55 (0.33, 0.92)	0.023	0.58 (0.34, 0.97)	0.037
Education				
Middle school and below	Ref.			
High school/technical secondary school	1.24 (0.66, 2.34)	0.501		
Junior college and above	0.51 (0.26, 1.00)	0.051		
Marital status				
Married	0.53 (0.25, 1.13)	0.100		
Unmarried/divorced/widowed	Ref.			
Childbirth				
Yes	0.88 (0.38, 2.05)	0.769		
No	Ref.			
Menopause				
Yes	0.98 (0.59, 1.62)	0.939		
No	Ref.			
Duration of breast cancer				
<3 years	Ref.			
≥3 years	1.08 (0.54, 2.14)	0.831		
Duration of chemotherapy for breast cancer				
<6 months	Ref.			
≥6 months	1.53 (0.84, 2.79)	0.163		
Chemotherapy-related neutropenia or febrile neutropenia				
Yes	1.33 (0.75, 2.36)	0.324		
No	Ref.			
Unclear	1.33 (0.69, 2.58)	0.392		

had incorrect knowledge regarding prevention and management of drug complication.[19] Pathirana *et al* found that only one-third of chemotherapy patients knew that premedication is giving before chemotherapy to manage side effects.[13] Previous studies have consistently identified gaps in patients' knowledge about preventive measures and risk factors, suggesting a critical need for improved patient education in these specific areas across different cancer populations.[20]

Despite the inadequate knowledge, our study found that the majority of breast cancer chemotherapy patients exhibited a positive attitude towards their treatment and preventive measures. This positive attitude echoes the findings of similar studies in cancer populations, where patients generally demonstrated a proactive and optimistic approach towards their treatment journey.[21–23] For instance, Jansen *et al* found that breast cancer patients, especially those with more experiences, had confidence in the positive outcomes of chemotherapy.[21] Furthermore, cancer patients reported positive attitude towards self-management.[23] However, the concern expressed by participants in our study over the financial burden associated with the treatment and prevention of neutropenia is a common issue faced by cancer patients in different settings.[24–26] In a study conducted in patients with breast and head and neck cancers, 69% had a significant or unmanageable financial burden of cancer.[24] Cancer-related financial burden was associated with lower health-related quality of life, and maladaptive coping can lead to poor health outcomes.[25 26] Financial considerations and healthcare costs can influence patients' adherence to recommended preventive measures, emphasising the importance of incorporating financial counselling and support services into comprehensive cancer care.

It is important to note that in our study, all cancer patients received related education before the start of

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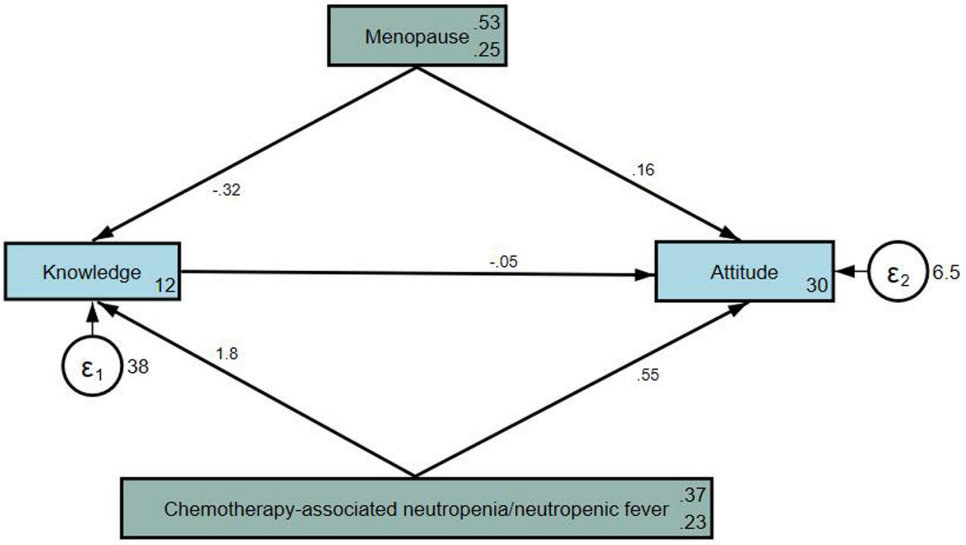

Figure 1 Structural equation model.

chemotherapy, which was provided at different centres but included all items from the practice section. However, replying on the questions in the practice section, a notable portion of participants reported that they were not informed. This suggests that received education was not sufficient and did not left the lasting impression on the patients, which could at least partly explain poor knowledge scores—new approaches to patient's education are urgently needed to bridge the observed gap. Higher levels of education were significantly associated with better knowledge scores, in line with previous research in various cancer populations, indicating that education plays a crucial role in shaping the patients' understanding of their treatment and potential complications.[27 28] However, SEM results in our study did not confirm the hypothesis that knowledge has a significant effect on attitudes, suggesting that knowledge alone might not be the sole driver of attitudes towards preventive measures. This finding aligns with some previous research, highlighting that other factors, such as emotional responses, fear or cultural beliefs, may also shape the patients' attitudes and behaviors.[29 30] The observed association between living in urban areas and a more negative attitude is another intriguing finding. While our study is the first to report such an association, it warrants further investigation and comparison with other studies. Understanding the reasons behind this disparity could help tailor interventions to address the specific needs and concerns of patients from urban areas.

This study has several limitations. First, due to the self-reporting nature of the study, the results might deviate from the actual practice. Second, there might be non-response bias from the use of online surveys and selection bias due to the inclusion criteria. Third, although the study was strengthened by the multi-centred design, future studies with a larger sample size are needed to confirm the study findings. Fourth, SEM was performed as a surrogate of causality, but such results must be taken with caution since causality is statistically inferred rather than observed;[31] thus, longitudinal studies could provide new insights into changes of KAP over time.

In conclusion, the patients had inadequate knowledge, positive attitude and suboptimal practice towards chemotherapy-related neutropenia and FN among breast cancer chemotherapy patients. The study also found that the level of education was significantly associated with adequate knowledge, and residence was significantly associated with positive attitude. It is important to design and implement effective education programmes to improve the KAP related to chemotherapy-related neutropenia and FN in this patient population. Patients with lower levels of knowledge and attitude (ie, patients with lower

Table 3 Estimates of hypothesis paths

	Direct effect		Indirect effect	
Model paths	**β (95% CI)**	**P**	**β (95% CI)**	**P**
Menopause → knowledge	−0.32 (−1.86, 1.22)	0.683	–	–
Chemotherapy-related neutropenia or febrile neutropenia → knowledge	1.77 (0.18, 3.36)	0.029		
Knowledge → attitude	−0.05 (−0.10, 0.002)	0.058	–	–
Menopause → attitude	0.16 (−0.48, 0.80)	0.618	0.02 (−0.06, 0.10)	0.689
Chemotherapy-related neutropenia or febrile neutropenia → attitude	0.55 (−0.11, 1.22)	0.103	−0.09 (−0.21, 0.03)	0.153

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levels of education) deserve more research and clinical attention.

Contributors YC: formal analysis, investigation, data curation, writing–original draft. HZ: conceptualisation, data curation, investigation, writing–original draft, methodology. JJ: supervision, visualisation, project administration, writing–review and editing. All authors read and approved the final manuscript. HZ acted as the guarantor.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Consent obtained directly from patient(s)

Ethics approval This work has been carried out in accordance with the Declaration of Helsinki (2000) of the World Medical Association. This study involves human participants and was approved by the Medical Ethics Committee of Quzhou People's Hospital (No. 2023-024). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data generated or analysed during this study are included in this published article.

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